

REMARKS

A. The Status of the Claims and the Amendments

Claims 116 and 164 have been amended. Claims 132-137, 142-145, 152-159, 161-163, 167, and 175-177 have been canceled without prejudice, as claims drawn to non-elected species. Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, and 178-184 are pending.

Claims 116 and 164 has been amended to define the Applicant's invention with greater precision, clarity and particularity. As amended, claims 116 and 164 are supported by the specification and the original claims and add no new matter. The support for the newly added limitation "cavitating and/or rupturing said vesicles" is found throughout the specification, e.g., at page 8, line 5; page 16, line 21; page 65, lines 14-16; and page 68, lines 1-11. It is submitted that the amendments place the claims in condition for allowance, or in better condition for appeal. Accordingly, entry of the amendments is respectfully requested.

B. Rejections Under 35 U.S.C. § 103(a)

Claims 116-131, 138-141, 146-151, and 160 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,695,460 to Siegel et al. (item 3, page 2 of the Office Action). This rejection is respectfully traversed on the following grounds.

To establish a *prima facie* case of obviousness, the three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference as proposed by the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference must teach or suggest all of the claim limitations. MPEP § 2143. Applicants submit that at least two of the above criteria have not been met.

Siegel et al. fail to describe a method which includes “cavitating and/or rupturing” vesicles “by applying to the patient ultrasonic energy having a frequency between about 750 kHz and 3 MHz,” as recited in claim 116. What Siegel et al. do describe instead is cavitating of vascular fluid (Col. 6, line 2). Nor is there any suggestion or motivation to modify the Siegel et al. reference to arrive at a claim which will contain every limitation of claim 116, because the frequencies employed by Siegel et al., while being sufficient to cause increased cavitation of the vascular fluid, are insufficient to cause “cavitating and/or rupturing” vesicles, as recited in claim 116.

The Applicant respectfully disagrees with the Examiner’s statement that Siegel et al. do not teach away from using ultrasound in the 750 KHz – 3 MHz frequency range, and to arrive to such range is a matter of mere “optimization.” Indeed, Siegel et al. clearly teach away from increasing the frequency of ultrasound by stating that “it has been found that when ultrasound is applied at a lower, **rather than a higher frequency**, the effectiveness of the method is markedly enhanced” (see, Col. 5, lines 29-31) (emphasis added). Siegel et al. also show that when the frequency is increased from 25 KHz to 243 KHz, the percentage of dissolved clots falls precipitously from $99 \pm 1 \%$ to just $26 \pm 6 \%$ (see, Col. 7, lines 54-57). Commenting on these results, Siegel et al. conclude that the “clot dissolution is significantly greater with lower frequencies, between about 25 and about 39 KHz, compared to higher frequencies” (see, Col. 7, lines 58-60).

The Applicants respectfully point out that the case law does not support the Examiner’s conclusions. In one case, also cited by the Examiner himself, the reference teaches away if the “line of development flowing from the reference ... is unlikely to be productive of the results sought by the applicant.” *In re Gurley*, 31 USPQ2d 1130, 1131-32 (Fed. Cir. 1994). It cannot be reasonably disputed that Siegel et al. teach that with the increase of frequency from 25 to 243 KHz, the results on clot dissolution worsen very substantially. Any further increase (“the line of development”) is likely to make the

results even worse and thus will not be productive of the improved results sought by the Applicants.

Therefore, it is submitted that one skilled in the art would not be motivated to modify the teachings of Siegel et al. towards the increase in frequency to 750 KHz or higher, because the teachings of Siegel et al. suggest that such modification will lead to even worse results..

Accordingly, claim 116 is patentably distinguishable over Siegel et al. Each of claims 117-131, 138-141, 146-151, and 160 all depend on claim 116 and are considered patentable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, and 178-184 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Siegel et al. in view of Porter (U.S. Patent No. 5,648,098) (item 5, page 6 of the Office Action). The rejection is respectfully traversed on the following grounds.

As mentioned above, Siegel et al. fail to describe a method which includes “cavitating and/or rupturing” vesicles “by applying to the patient ultrasonic energy having a frequency between about 750 kHz and 3 MHz,” as recited in claim 116. Siegel et al. also fail to describe a method which includes “activating said acoustically active composition by applying to the patient ultrasonic energy having a frequency between about 750 kHz and 3 MHz,” as recited in claim 164. Porter fails to cure this deficiency.

As discussed above, Siegel et al. disclose that ultrasound should not be applied at frequencies higher than about 100 kHz (Col. 5, lines 32-34), because the best results will be achieved at the frequencies below 100 KHz, e.g., 25-53 KHz. Porter discloses the ultrasound frequencies of “20 kHz to several MHz” (Col. 4, lines 48-49).

It is submitted that the teachings of Siegel et al. cannot be combined for the frequencies above 100 KHz, because Siegel et al. describe that using frequencies above 100 KHz will lead to less satisfactory results. If the disclosure of Porter is used, using any frequency disclosed by Porter which is over 100 kHz will be in conflict with what is taught by Siegel et al. Accordingly, there is no motivation to combine Siegel et al. and Porter.

Accordingly, it is submitted that claims 116 and 164 are patentably distinguishable over the combination of Siegel et al. and Porter. Claims 117-131, 138-141, 146-151 and 160 depend, directly or indirectly on claim 116 and are considered patentable for at least the same reason. Claims 165, 166, 168-174, and 178-184 depend, directly or indirectly on claim 164 and are considered patentable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,



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